# Perfluorochemical modification of the fetal membranes: potential molecular mechanisms driving spontaneous preterm birth

**Kristin D. Gerson, MD, PhD**

**Abstract**

Pregnancy represents a critical window of susceptibility during which environmental exposures carry potential to impact reproductive outcomes, including preterm birth (PTB). Etiologies of spontaneous PTB are incompletely understood though frequently involve inflammatory events converging upon preterm premature rupture of membranes (PPROM) and premature cervical remodeling. Epidemiologic studies focused on environmental exposures and PTB have identified a role for perfluorochemicals (PFCs) and their replacement compounds. Termed “forever chemicals” due to their long half-life, PFCs are commonly used in consumer products and elevated in maternal serum, cord blood, and amniotic fluid among individuals with PTB. Outside of pregnancy, PFCs can induce immune dysfunction. Whether these chemicals play a mechanistic role in PPROM and cervical remodeling remains uninvestigated. The overall goal of this proposal is to elucidate the molecular effects of PFCs on fetal membranes and cervical remodeling. Our central hypothesis is that PFCs induce immune dysfunction contributing to PPROM, and that these events drive cervical remodeling through immune crosstalk between the fetal membranes and cervix. We propose the following aims: 1) quantify associations between PFC concentrations in fetal membranes and PPROM; 2) determine how PFCs modify molecular profiles in fetal membranes; and 3) determine how PFC exposure of fetal membranes modifies cervical remodeling. In the first aim, we will leverage fetal membranes from a completed pregnancy cohort to quantify PFC concentrations in PPROM cases versus term birth controls by mass spectrometry. For the second aim, we will generate fetal membrane explants to establish how PFCs modify transcriptional profiles using RNA-Seq, as well as NF-KB-mediated immune responses by Luminex and inflammasome activation. In the third aim, we will test the ability of PFC-exposed fetal membrane explants to induce barrier dysfunction in endocervical cells. Our proposal is highly innovative, pioneering mechanistic studies to investigate the effects of ubiquitous environmental toxicants in understudied reproductive tissues.